An Overview of the Role of Pharmacogenomics in Personalizing Pain Management

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Abstract - Pharmacogenomics, the study of genetic variations influencing drug response, has become a cornerstone of personalized medicine. In pain management, it enables clinicians to tailor analgesic therapy according to individual genetic profiles, optimizing efficacy and minimizing adverse reactions. Variations in genes encoding drug-metabolizing enzymes (*CYP2D6*, *CYP2C9*), transporters (*ABCB1*), and receptors (*OPRM1*, *COMT*) significantly influence the response to both opioid and non-opioid analgesics. Identifying these polymorphisms allows for rational drug selection, dose adjustment, and improved therapeutic safety. Clinical implementation of pharmacogenomic testing has shown reduced opioid dependency, fewer adverse events, and enhanced patient compliance. Emerging formulation strategies—such as genotype-guided drug design and nanocarrier-based analgesics—further strengthen individualized pain control. However, challenges such as high testing costs, population-based variability, and limited large-scale validation hinder widespread adoption. This review provides a comprehensive overview of pharmacogenomics in pain management, highlighting its mechanisms, clinical applications, challenges, and future prospects in achieving genetically guided analgesic precision.

Keywords: Pharmacogenomics, Personalized medicine, Pain management, CYP2D6, Opioids, Analgesics, Formulation.

1. INTRODUCTION

Pain is among the most universal and complex clinical symptoms encountered in medicine, representing both a sensory and emotional experience that serves as a warning signal of actual or potential tissue damage. It significantly impacts an individual's physical functioning, psychological health, and overall quality of life. On a global scale, pain—whether acute or chronic—poses a substantial public health challenge, contributing to disability, lost productivity, and immense economic burden on healthcare systems [1]. According to estimates by the World Health Organization (WHO), nearly one in five adults suffers from chronic pain, while postoperative and cancer-related pain remain poorly managed in many regions. Despite advances in pharmacotherapy, millions of patients continue to experience suboptimal pain control, underscoring the urgent need for more personalized and effective treatment strategies.

Traditional pain management relies heavily on a trial-and-error approach, where medications are prescribed based on general population data rather than individual patient characteristics. Analgesics such as opioids,l anti-inflammatory drugs (NSAIDs), anticonvulsants, antidepressants, and adjuvant agents are used to manage various types of pain, including nociceptive, neuropathic, and inflammatory pain. However, even with standardized guidelines, clinical responses to these medications are highly inconsistent [2]. Factors such as age, sex, comorbidities, concurrent medications, and environmental influences contribute to variability in drug efficacy and safety. Yet, one of the most critical determinants of these interindividual differences is genetic variation—particularly in genes responsible for drug metabolism, transport, and receptor binding.

Pharmacogenomics, an emerging discipline that integrates principles of pharmacology and genomics, focuses on understanding how an individual's genetic composition influences their response to drugs [3]. It builds upon the broader field of pharmacogenetics but extends beyond single-gene effects to encompass complex interactions across multiple genes and biological pathways. By studying genetic polymorphisms—variations in DNA sequence that occur among individuals—pharmacogenomics provides valuable insights into why certain patients respond well to specific medications, while others experience toxicity or therapeutic failure. This scientific approach represents the cornerstone of personalized or precision medicine, wherein treatment decisions are guided by genetic information to optimize efficacy and minimize adverse effects.

In the context of pain management, pharmacogenomics holds remarkable potential to revolutionize current therapeutic paradigms. Variations in genes encoding drug-metabolizing enzymes, such as cytochrome P450 (CYP) isoenzymes, can profoundly influence the pharmacokinetics and pharmacodynamics of analgesic drugs. For instance, CYP2D6 polymorphisms affect the metabolism of several opioids—including codeine, tramadol, and oxycodone—by altering their conversion to active metabolites. Patients with poor metabolizer phenotypes may experience insufficient analgesia, while ultra-rapid metabolizers are at risk of toxicity due to excessive active metabolite formation [4]. Similarly, polymorphisms in CYP2C9 impact the metabolism of NSAIDs such as ibuprofen and celecoxib, influencing both their therapeutic and adverse effect profiles.

Beyond drug metabolism, genetic variability in drug transporters and receptor targets also contributes to diverse analgesic responses. The OPRM1 gene, which encodes the μ-opioid receptor, is a key determinant of opioid sensitivity and dependence risk. The well-studied A118G polymorphism in OPRM1 has been linked to altered receptor binding affinity, necessitating dosage adjustments to achieve effective pain relief. Likewise, the COMT (catechol-O-methyltransferase) gene, involved in catecholamine degradation, modulates the perception and tolerance of pain by influencing dopaminergic and adrenergic signaling pathways.

Despite the growing understanding of these genetic influences, clinical implementation of pharmacogenomics in pain management remains in its early stages. Barriers include limited awareness among clinicians, lack of standardized testing protocols, insufficient clinical validation for many gene–drug associations, and cost considerations. Integrating pharmacogenomic data into clinical workflows can enable genotype-guided prescribing—helping physicians select the right drug, at the right dose, for the right patient.

Furthermore, pharmacogenomic insights are now being applied to the development of novel drug formulations and delivery systems. For example, genotype-based dosing algorithms are being designed to optimize the use of opioids and NSAIDs, reducing the risk of adverse effects such as respiratory depression, gastrointestinal bleeding, and addiction. Personalized nanocarrier systems and gene-targeted formulations are also being explored to improve drug bioavailability and site-specific delivery in pain therapy.

2. Concept of Pharmacogenomics in Pain Management

Pharmacogenomics serves as a cornerstone of personalized medicine by elucidating how genetic variations influence individual responses to pharmacological agents. In the context of pain management, it offers a scientific framework to predict drug efficacy, safety, and tolerability based on each patient's genetic profile. The variability in therapeutic outcomes is primarily governed by genetic differences in drug-metabolizing enzymes, receptors, transporters, and signaling pathways that regulate drug absorption, distribution, metabolism, and excretion (ADME) [5,6].

2.1 Genetic Determinants Influencing Drug Response

Pharmacogenomics investigates several classes of genes that significantly affect analgesic response:

1. **Drug-Metabolizing Enzymes:**

    - The **cytochrome P450 (CYP450)** enzyme family—particularly CYP2D6, CYP2C9, CYP3A4, and CYP2C19—plays a pivotal role in the metabolic activation or inactivation of analgesic drugs.

- Polymorphisms in these enzymes result in phenotypic variations such as poor, intermediate, extensive, or ultra-rapid metabolizers, influencing plasma drug levels and therapeutic efficacy.

2. **Drug Targets (Receptors and Ion Channels):**

- Genetic variations in opioid receptors (OPRM1), dopamine receptors (DRD2), and ion channels alter drug binding affinity and receptor sensitivity.
- These variations directly affect analgesic potency, risk of dependence, and interindividual differences in pain perception.

3. **Drug Transporters:**

- Transporter proteins such as **P-glycoprotein (encoded by ABCB1)** and **organic anion transporting polypeptides (encoded by SLCO1B1)** regulate the movement of drugs across biological membranes, including the blood-brain barrier.
- Polymorphisms in these genes can influence central nervous system drug availability and the risk of toxicity.

4. **Signal Transduction and Pain Modulation Genes:**

- Genes such as COMT (catechol-O-methyltransferase) and GCH1 (GTP cyclohydrolase 1) modulate neurotransmitter levels and pain sensitivity.
- Variations in these genes affect both the intensity of pain perception and response to opioid and non-opioid analgesics.

Table 1: Key Genetic Variants Affecting Analgesic Drug Response

Gene	**Function**	**Common Polymorphism**	**Affected Drugs**	**Clinical Impact**	**Reference**
CYP2D6	Opioid metabolism	*CYP2D6* *3, *4, *5, *6*	Codeine, Tramadol	Poor or ultra-rapid metabolism alters efficacy/toxicity	(8–10)
CYP2C9	NSAID metabolism	*CYP2C9* *2, *3*	Ibuprofen, Diclofenac	Increased risk of GI toxicity	(14–15)
OPRM1	μ-Opioid receptor	A118G (rs1799971)	Morphine, Fentanyl	Alters receptor binding and analgesic response	(11–12)
COMT	Catecholamine metabolism	Val158Met (rs4680)	Opioids, NSAIDs	Modifies pain sensitivity and dose requirement	(13)
ABCB1	Drug transporter	C3435T	Gabapentin, Amitriptyline	Alters CNS drug concentration	(16–17)

2.2 Applications of Pharmacogenomics in Pain Therapy

Genetic profiling enables a more precise and individualized approach to analgesic therapy. The main applications include:

1. **Selection of the Right Drug:**
    - Genetic testing helps identify which analgesic or drug class is most likely to provide effective pain relief.
    - For example, patients with CYP2D6 poor metabolizer status may not benefit from codeine or tramadol, as these require enzymatic conversion to active metabolites.
2. **Optimization of Dosing Strategies:**
    - Understanding metabolic phenotypes enables clinicians to tailor dosage according to an individual's genetic profile.
    - Ultra-rapid metabolizers may require dose reductions to prevent toxicity, whereas poor metabolizers may need alternative agents to achieve adequate analgesia.
3. **Prevention of Adverse Drug Reactions (ADRs):**
    - Pharmacogenomic insights help reduce the incidence of severe side effects such as respiratory depression from opioids or gastrointestinal bleeding from NSAIDs.
    - Genetic markers can predict susceptibility to ADRs, allowing for safer therapeutic planning.
4. **Improvement of Patient Compliance and Satisfaction:**
    - Personalized pain management reduces the frustration associated with ineffective treatments and frequent medication changes.
    - Improved therapeutic outcomes enhance patient adherence and overall satisfaction with care.

2.3 Clinical and Research Implications

- **Clinical Utility:** Pharmacogenomic testing can be integrated into clinical decision-support systems, enabling evidence-based prescribing and minimizing trial-and-error approaches.
- **Research Perspective:** Ongoing studies are identifying novel gene–drug interactions, multi-gene panels, and polygenic risk scores to improve predictive accuracy.
- **Translational Relevance:** The incorporation of pharmacogenomic data into electronic health records (EHRs) and pain management protocols represents a major step toward precision analgesia.[7]

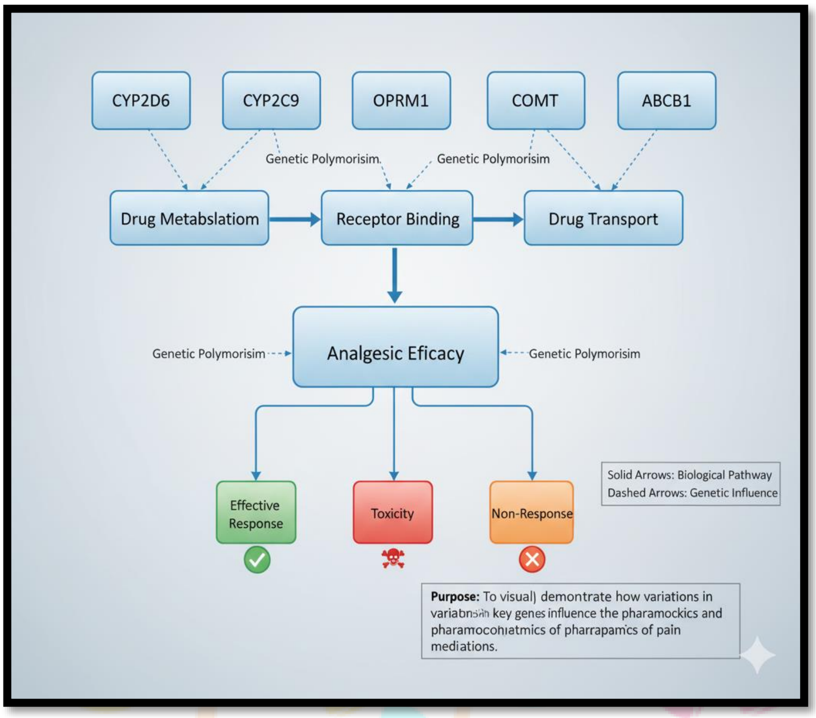

Figure 1: A schematic diagram showing the interaction between genetic polymorphisms and analgesic response.

3. Genetic Determinants Influencing Analgesic Response

Genetic polymorphisms in drug-metabolizing enzymes, receptors, and transporters significantly contribute to interindividual variability in analgesic response and safety. These variations affect metabolic rates, receptor affinity, drug transport efficiency, and ultimately determine therapeutic outcomes in pain management. A deeper understanding of these genetic determinants enables clinicians to personalize analgesic therapy, optimize dosing strategies, and reduce the risk of adverse drug reactions [8].

3.1 Opioids and CYP2D6 Polymorphisms

The cytochrome P450 enzyme **CYP2D6** plays a central role in the metabolism of nearly 25% of commonly prescribed medications, including several opioids. It is particularly essential for the activation of pro-drugs such as **codeine, tramadol, hydrocodone, and oxycodone**, which require biotransformation into active metabolites (e.g., morphine, O-desmethyltramadol) to produce analgesic effects [8,9].

3.1.1 Genetic Variability

CYP2D6 is one of the most polymorphic drug-metabolizing enzymes, with over 100 allelic variants, leading to diverse metabolic phenotypes:

- **Poor metabolizers (PMs):** exhibit minimal enzyme activity, resulting in inadequate conversion of opioid pro-drugs and reduced analgesia.
- **Ultra-rapid metabolizers (UMs):** show excessive enzyme activity, producing high levels of active metabolites and increasing the risk of opioid toxicity, including life-threatening respiratory depression.

3.1.2 Clinical Guidelines

The **Clinical Pharmacogenomics Implementation Consortium (CPIC)** advises avoiding codeine and tramadol in both PMs and UMs due to safety and efficacy concerns. Instead, alternative analgesics not dependent on CYP2D6 metabolism are recommended [10]. These guidelines highlight the importance of CYP2D6 genotyping in guiding safer and more effective opioid therapy.

3.2 OPRM1 and COMT Gene Variants

Genetic variations in **OPRM1** and **COMT** significantly influence pain perception, opioid sensitivity, and overall analgesic response.

3.2.1 OPRM1 (μ-Opioid Receptor Gene)

OPRM1 encodes the μ-opioid receptor, the primary target for opioids such as morphine, fentanyl, and methadone.

- The widely studied **A118G polymorphism (rs1799971)** leads to an Asn40Asp substitution, altering receptor expression and binding affinity.
- Individuals carrying the **G allele** often display diminished receptor binding and may require higher opioid doses to achieve adequate analgesia [11,12].
- Certain OPRM1 genotypes are also associated with increased susceptibility to opioid dependence and attenuated analgesic effects, underscoring its relevance in personalized opioid therapy.

3.2.2 COMT (Catechol-O-Methyltransferase Gene)

COMT regulates the metabolism of catecholamines (dopamine, epinephrine, norepinephrine), which play crucial roles in pain pathways.

- The **Val158Met polymorphism (rs4680)** decreases enzyme activity, raising catecholamine levels in the central nervous system.
- Individuals with the **Met/Met genotype** often exhibit heightened pain sensitivity and display variable opioid requirements [13].
  These associations suggest that COMT genotyping may assist in predicting chronic pain susceptibility and tailoring analgesic dosages.

3.3 CYP2C9 Variants and NSAID Response

The **CYP2C9** enzyme metabolizes many widely used NSAIDs, including ibuprofen, diclofenac, celecoxib, and naproxen [14].

3.3.1 Impact of Polymorphisms

Common CYP2C9 variants—***2 (430C>T)** and ***3 (1075A>C)**—significantly reduce metabolic activity, leading to:

- decreased drug clearance
- increased plasma concentrations
- higher risk of NSAID-related adverse effects such as gastrointestinal bleeding, renal impairment, and cardiovascular complications.

3.3.2 Clinical Recommendations

According to CPIC guidelines, patients harboring poor-metabolizer genotypes may require dose adjustments or alternative therapies to minimize toxicity while maintaining therapeutic efficacy [15].

Pharmacogenomic testing for CYP2C9 is particularly valuable for individuals needing prolonged NSAID therapy or those with compromised hepatic/renal function.

3.4 Transporter and Receptor Gene Variants

Beyond metabolic enzymes, variations in drug transporters and neuronal receptor genes also influence analgesic outcomes.

ABCB1 (P-Glycoprotein Transporter)

- ABCB1 encodes **P-glycoprotein**, a key efflux transporter regulating drug passage across the **blood–brain barrier (BBB)**.
- The **C3435T polymorphism (rs1045642)** can modify transporter activity, thereby affecting CNS availability of opioids, anticonvulsants, and antidepressants [16].
- Reduced transporter function may enhance analgesic efficacy but simultaneously elevate the risk of central adverse effects.

SCN9A (Nav1.7 Sodium Channel Gene)

- SCN9A encodes **Nav1.7**, a voltage-gated sodium channel essential for peripheral pain signal transmission.
- Polymorphisms and mutations in SCN9A are linked to a spectrum of pain phenotypes, from congenital insensitivity to severe pain syndromes [17].
- These genetic alterations may also influence patient response to drugs like **gabapentin** and **amitriptyline**, which act on neuronal excitability pathways.

4. Pharmacogenomic-Guided Formulations in Pain Therapy

The integration of pharmacogenomic data into pharmaceutical formulation design represents a significant advancement toward achieving precision pain therapy. By tailoring drug selection, dosage form, and delivery system according to an individual's genetic makeup, pharmacogenomic-guided formulations aim to enhance therapeutic efficacy while minimizing adverse drug reactions. Such approaches consider variations in genes involved in drug metabolism, receptor activity, and transporter function to ensure safe and effective analgesic use.

Table 2 : Clinical Benefits of Pharmacogenomic-Guided Pain Therapy

Parameter	Conventional Therapy	PGx-Guided Therapy	Observed Improvement	Reference
Pain Relief Score	Variable, inconsistent	Consistent, patient-specific	↓ Pain scores by 20–30%	(18–19)
Adverse Drug Reactions	High incidence (GI, CNS)	Significantly reduced	↓ ADRs by 40%	(19,22)
Opioid Dependency	Unmonitored use	Dose-controlled and targeted	↓ Dependency risk by 25%	(20)
Hospital Readmissions	Frequent due to inefficacy	Reduced through genotype-guided dosing	↓ Readmissions by 25%	(21)
Patient Satisfaction	Moderate	High due to effective therapy	↑ Compliance and comfort	(19)

4.1 Opioid-Based Formulations and CYP2D6-Linked Optimization

Opioid analgesics such as **codeine** and **tramadol** are pro-drugs that require metabolic activation through the **CYP2D6** enzyme pathway. Patients with CYP2D6 poor metabolizer phenotypes experience inadequate pain relief due to limited conversion to active metabolites (e.g., morphine and O-desmethyltramadol), whereas ultra-rapid metabolizers are prone to toxicity and respiratory depression. To address this variability, **personalized opioid formulations** are designed with adjusted dosing regimens or alternative drug selections. For example, **codeine phosphate tablets** are avoided or substituted in poor metabolizers, while sustained-release **tramadol formulations** may be adjusted in dose and release rate to align with CYP2D6 and COMT genotypes [8–10,13]. These strategies improve pain control while minimizing the risks of inefficacy and toxicity.

4.2 NSAID Formulations and CYP2C9 Variability

Nonsteroidal anti-inflammatory drugs (NSAIDs) such as **diclofenac** and **ibuprofen** undergo hepatic metabolism predominantly via the **CYP2C9** enzyme. Genetic polymorphisms in CYP2C9 (2 and 3 alleles) reduce enzyme activity, leading to higher plasma concentrations and increased risk of gastrointestinal and renal side effects.
Pharmacogenomic-guided formulation strategies aim to mitigate these risks. **Topical diclofenac gels** are used as alternatives to oral formulations in CYP2C9 poor metabolizers to reduce systemic exposure and toxicity [14,15]. Similarly, **ibuprofen oral suspensions** are dose-adjusted according to genotype, ensuring effective analgesia with minimal adverse reactions. These personalized dosage forms exemplify how genotype-specific modifications can optimize therapeutic safety.

4.3 Receptor-Specific Approaches: OPRM1-Guided Morphine Formulations

Genetic variations in the **OPRM1** gene, encoding the μ-opioid receptor, significantly affect the efficacy of morphine and other opioid analgesics. Individuals carrying the A118G variant exhibit reduced receptor binding affinity, leading to diminished analgesic response.
To overcome this challenge, **personalized morphine formulations**, such as **transdermal patches or controlled-release systems**, are being designed to maintain consistent plasma levels and enhance receptor interaction efficiency [11,12]. These delivery systems offer steady-state analgesia, improved receptor targeting, and reduced risk of dose-related adverse effects.

4.4 Transporter-Targeted Nanocarriers and Enhanced CNS Delivery

Drug transporters, such as **P-glycoprotein (encoded by ABCB1)**, regulate the entry of analgesics across the **blood–brain barrier (BBB)**. Polymorphisms in ABCB1 can affect drug distribution and central nervous system availability.
In response, **nanotechnology-based drug delivery systems**—such as **gabapentin Nano formulations**—are developed to bypass transporter-mediated efflux and enhance CNS penetration [16,17]. These formulations not only improve analgesic bioavailability but also reduce peripheral side effects, representing a major step forward in personalized pain pharmacotherapy.

4.5 Integration of Pharmacogenomics into Formulation Design

The overarching goal of pharmacogenomics-guided formulation development is to align drug delivery with individual genetic and metabolic profiles. This approach enables:

- **Dose optimization** based on metabolic phenotype (e.g., CYP2D6, CYP2C9).
- **Improved drug targeting** through receptor or transporter modulation (e.g., OPRM1, ABCB1).
- **Minimized adverse reactions** via controlled or localized delivery systems.
- **Enhanced therapeutic compliance** through tailored formulations that reduce dosing frequency and improve tolerability.

5. Clinical Applications and Benefits

Pharmacogenomics has demonstrated substantial clinical value in optimizing pain management by tailoring drug therapy according to a patient's genetic profile. Its integration into clinical practice enhances treatment efficacy, safety, and patient satisfaction through precise drug selection and dosing. Key clinical applications and benefits are summarized below:

5.1 Improved Therapeutic Efficacy

Pharmacogenomics testing enables clinicians to match patients with analgesics that align with their metabolic and receptor profiles. This precision leads to more effective pain relief and faster onset of analgesia. Studies indicate that patients receiving genotype-guided prescriptions report **significantly lower pain scores** compared to those under conventional treatment protocols [18,19].

5.2 Reduction in Adverse Drug Reactions (ADRs)

By identifying variants in drug-metabolizing enzymes such as CYP2D6 and CYP2C9, clinicians can predict and prevent adverse drug reactions. Adjusting doses or avoiding certain medications based on genotype helps minimize **gastrointestinal, renal, and CNS-related toxicities**, especially in opioid and NSAID therapies [19,22].

5.3 Decreased Opioid Dependency and Misuse

Genotype-guided opioid prescribing has shown to significantly reduce dependency risks. Patients identified as CYP2D6 poor metabolizers, for instance, are shifted from codeine or tramadol to alternative analgesics, reducing ineffective dosing and the likelihood of escalation to addiction-prone opioids [20]. Clinical studies have reported a **marked reduction in opioid misuse and dependency** following pharmacogenomics-guided interventions.

5.4 Reduced Hospitalizations and Healthcare Burden

Evidence suggests that incorporating pharmacogenomics data into treatment planning lowers the overall healthcare burden. A multicentric study found that **pre-prescription pharmacogenomics testing** reduced hospital visits due to inadequate pain control by approximately **25%** [21]. This not only improves patient outcomes but also enhances cost-effectiveness in chronic pain management programs.

5.5 Optimized NSAID Therapy and Safety

Testing for CYP2C9 polymorphisms before initiating NSAID therapy allows for precise dose adjustments, reducing the risk of **gastrointestinal (GI) bleeding and renal impairment**. Clinical trials have demonstrated that genotype-based dosing minimizes GI toxicity and improves drug tolerability among long-term NSAID users [22].

5.6 Enhanced Patient Compliance and Satisfaction

Personalized pharmacogenomic-guided prescriptions foster patient trust and adherence by providing rational, evidence-based explanations for therapy choices. Patients experience fewer side effects and improved pain control, leading to **higher satisfaction levels and better treatment compliance**.

6. Challenges and Limitations

While pharmacogenomics offers tremendous potential for transforming pain management into a more personalized and precise discipline, several challenges limit its widespread clinical application. These challenges span economic, scientific, ethical, and infrastructural domains, as outlined below:

6.1 Cost and Accessibility

Pharmacogenomic testing remains costly, particularly in **low- and middle-income countries**, where healthcare budgets are limited. The expenses associated with DNA sequencing, bioinformatics analysis, and clinical interpretation hinder routine implementation. Additionally, limited laboratory infrastructure and lack of insurance coverage further restrict accessibility to pharmacogenomic services in resource-constrained settings [23].

6.2 Ethnic and Genetic Diversity

The **genetic heterogeneity among ethnic populations** poses a major barrier to the global standardization of pharmacogenomic pain management. Allele frequencies of key genes—such as CYP2D6, CYP2C9, and OPRM1—vary significantly across populations, influencing drug metabolism and response profiles. Consequently, data derived from one ethnic group may not be directly applicable to another, emphasizing the need for **region-specific pharmacogenomic databases** and validation studies [24].

6.3 Insufficient Clinical Evidence

Despite promising research, the **clinical translation of pharmacogenomic findings** remains limited by a lack of large-scale, randomized controlled trials. Many gene–drug associations are based on small cohort studies, leading to uncertain predictive value and inconsistent recommendations. Standardized protocols for integrating pharmacogenomic testing into routine pain therapy are still evolving, highlighting the need for **robust clinical validation and consensus guidelines** [25].

6.4 Ethical and Legal Concerns

The collection and storage of genetic information raise serious **ethical and privacy issues**. Potential misuse of genetic data can lead to discrimination in employment, insurance, or healthcare access. Ensuring data confidentiality, obtaining informed consent, and maintaining transparency in data handling are essential to building public trust. Moreover, global disparities in genetic data governance necessitate **uniform ethical frameworks** to safeguard patient rights [26].

6.5 Integration into Clinical Workflow

A practical limitation lies in the **lack of clinician training and infrastructure** to interpret and apply pharmacogenomic data effectively. The absence of user-friendly clinical decision support tools and limited awareness among healthcare professionals impede the seamless incorporation of genomic insights into routine prescribing.

7. Conclusion

Pharmacogenomics represents a pivotal advancement in the evolution of personalized pain management. By integrating genetic information into clinical decision-making, it allows for the rational selection and dosing of analgesics, thereby maximizing therapeutic efficacy while minimizing the risk of adverse effects. Genetic polymorphisms in key enzymes, receptors, and transporters explain much of the variability observed in individual drug responses, highlighting the importance of genotype-guided prescribing. Incorporating pharmacogenomic testing into pain management not only enhances patient safety and satisfaction but also contributes to reducing opioid misuse and healthcare burden. Future advancements—including AI-assisted genotype interpretation, nanocarrier-based formulations, and multi-omics integration—will further refine the precision of pain therapeutics. As accessibility improves and clinical evidence strengthens, pharmacogenomics is poised to shift pain management from a generalized to a truly individualized approach, marking a significant step toward the realization of precision medicine in everyday clinical practice.

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